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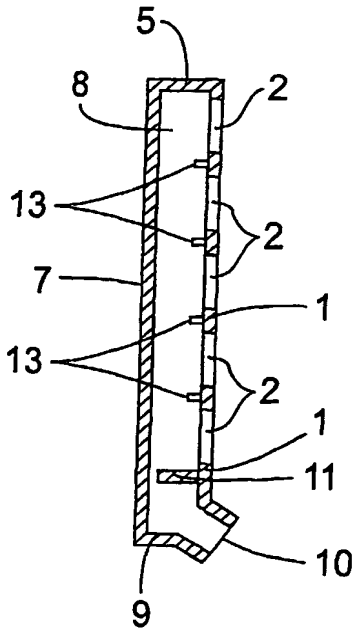
(54) Title: HOLDER AND METHOD FOR COOLING OR HEATING SAMPLES



(57) Abstract: A holder for a microtitreplate or an array of separate test tubes comprising a first panel (1) provided with a recess (2) for receiving each well (3) of the microtitreplate or test tubes and a second panel (7), which together with the first panel (1) and three side walls (5) form an inner space (8). The fourth side (9) comprises an inlet (10) for gas or liquid, whereby the gas or liquid entering the inner space (8) via the inlet (10) leaves the inner space (8) via said recesses (2), along the outside of the wells (3). A method for cooling or heating samples contained in wells (3) of a microtitreplate or an array of separate test tubes by inserting the microtitreplate or array of separate test tubes into such a holder and letting gas or liquid enter said inner space (8).

WO 2004/056485 A1

HOLDER AND METHOD FOR COOLING OR HEATING SAMPLES

The present invention concerns a holder for a microtitreplate or for an array of separate test tubes and a method for cooling or heating samples contained in the wells of a microtitreplate or an array of separate test tubes.

Background

In order to speed up chemical testing procedures there is an increasing demand for making manifold analyses in parallel. In typical cases such parallel analyses are performed in an array of separate test tubes or in different wells of a single unit called a microtitre plate.

A problem with such an approach arises during incubation, that is, when the samples are heated or cooled to desired reaction temperatures, which use to be referred to as "well-to-well uniformity". The problem is to expose the separate tubes or wells uniformly for the heating and cooling medium, often a gas or a liquid and to obtain homogeneous temperature within this medium.

The major source of poor thermal uniformity is the temperature gradients commonly established from the edges to the center of the tube array or the microtitre plate. Such gradients are more severe if the tubes or wells are obstacles for the flow of the medium, which often is the case.

Summary of the invention

The present invention aims to alleviate the above problems. The solution is provided by means of a holder according to claim 1 and a method according to claim 6.

An advantage with this is that the cooling or heating gas or liquid is spread evenly around each well providing a uniform heating or cooling of each sample in the microtitreplate or test tubes of the array.

The holder and method according to the present invention are especially advantageous when centrifuging microtitreplates or arrays of separate test tubes, for example, in a thermocycling device.

Tests have shown that systematic differences in temperature in the sample when using know technique to cool or heat samples in a microtitreplate or in an array of separate test tubes have been eliminated when using the present invention. Any small remaining differences are random instead of systematic.

Short description of the drawings

The present invention will now be described by means of exemplifying embodiments in connection with the sketch drawings, in which:

Fig. 1 illustrates in a plan view a holder according to an embodiment of the present invention.

Fig. 2 illustrates in a cross sectional side view the holder according to Fig. 1.

Fig. 3 illustrates in a cross sectional side view a holder according to an embodiment of the present invention with a microtitreplate arranged therein.

Fig. 4 illustrates in a plan view a detail of the holder with a microtitreplate arranged therein according to Fig. 1.

Fig. 5 illustrates in a cross sectional view an embodiment of a recess.

Fig. 6 illustrates in a cross sectional view another embodiment of a recess.

Detailed description of preferred embodiments

A holder according to the present invention comprises a first panel 1, which preferably is substantially flat and for example made of a polymer material. The first panel 1 is provided with a number of recesses 2 adapted for receiving a well 3 of a microtitreplate 12 or a separate test tube. Preferably the number of recesses 2 corresponds to the number of wells 3 in a microtitreplate 12, for example 96.

The recesses 2 may be through holes as illustrated in Figs. 1-4 or dents or funnels as illustrated in Figs. 5 and 6, respectively, having a hole in the bottom for gas or liquid to flow therethrough. Preferably the recesses 2

may have a shape of a circle, but may instead have shapes of an ellipse, square, rectangle or an octagon for example (not shown).

The first panel 1 has preferably a rectangular shape substantially corresponding to a microtitreplate 12. Along three of the edges 4 of the first panel 1 a side wall 5 is provided, which together with a second panel 7 forms an inner space 8 in the holder. The fourth edge 9 comprises an inlet opening 10 for cooling or heating gas or liquid.

The second panel 7 is preferably in the form of a lid, which is releasable attached, so that a microtitreplate 12 or separate test tubes may be inserted into the holder and the holder is closed by means of said lid 7 and thus forming the inner space 8, see Fig 2. The lid 7 may be positioned so as to cover all the inlets of the wells 3 or be formed by a microtitreplate 12 itself as illustrated in Fig. 3.

The inlet opening 10 may extend along the whole side 9 of the first panel 10 or comprise several subopenings or extend along a part of the side 9 or be adapted in a suitable way for the specific use.

When cooling or heating the samples contained in the wells 3 cold or hot gas or liquid is made to flow into the inlet 10 of the holder so that the gas or liquid will flow around the upper portions of the wells 3 and fill the inner space 8. See arrows in Fig. 3.

The gas or liquid will then flow from the inner space 8 via gaps 6 between the recesses 2 and the wells 3 and further along the outside of the wells 3, thereby cooling

or heating the samples inside the wells (3) in a homogeneous way.

In order to make sure that a gap 6 is provided between the recess 2 and the well 3, the edge may be provided with one or more protrusions 13, see Figs. 2 and 4, protruding into the middle of the recess 2 or protruding from the inner side of the first panel 1, i.e. the side facing the microtitreplate 12 when it is arranged in the holder.

In case of the recesses 2 having a shape of a ellipse, for example, the protrusions may be missed out since the wells 3 would come into contact with the recesses 2 at two points of the elongated sides of the ellipse but there would still be a gap 6 around the rest of the circumference of the well 3.

Due to this or these protrusions 13 the microtitreplate 12 or the separate test tubes arranged in an array are prevented from reaching too close to the first side panel 1 so that the wells 3 would fill the whole recesses 2 and thus preventing the cooling or heating gas or liquid from flowing through the gap 6 along the outside of the wells 3.

In front of a first row of wells 3 of a microtitreplate 12 or an array of test tubes, seen in the flow direction, one or more baffles 11 may be arranged in order to spread the gas or liquid more evenly in the inner space 8 so that the first row will not be "hit" by all of the gas or liquid. See Fig. 2.

CLAIMS

1. A holder for a microtitreplate (12) or an array of separate test tubes, **characterised in** that it comprises a first panel (1) provided with a recess (2) for receiving each well (3) of the microtitreplate (12) or test tubes and a second panel (7), which together with the first panel (1) and three side walls (5) form an inner space (8), wherein the fourth side (9) comprises an inlet (10) for gas or liquid, whereby the gas or liquid entering the inner space (8) via the inlet (10) leaves the inner space (8) via said recesses (2), along the outside of the wells (3).

2. A holder according to claim 1, wherein the second panel (7) is made up by the microtitreplate (12) itself.

3. A holder according to claim 1, wherein the second panel (7) is a releasable lid.

4. A holder according to claim 1, 2 or 3, wherein at least one protrusion (13) is provided on the first panel (1) in order to secure a gap (6) between the wells (3) and the recesses (2).

5. A holder according to anyone of the previous claims, wherein at least one baffle (11) is provided in front of the row of wells (3) positioned closest to the inlet (10) for gas or liquid.

6. A method for cooling or heating samples contained in wells (3) of a microtitreplate (12) or an array of separate test tubes, **characterised by** inserting the microtitreplate (12) or array of separate test tubes into a holder comprising a first panel (1) provided with a recess (2) for receiving each well (3) of the microtitreplate (12) or test tubes and a second panel (7), which together with the first panel (1) and three side walls (5) form an inner space (8), wherein the fourth side (9) comprises an inlet (10) for gas or liquid, and letting gas or liquid enter said inner space (8) of the holder and further out through said recesses (2), along the outside of the wells (3).

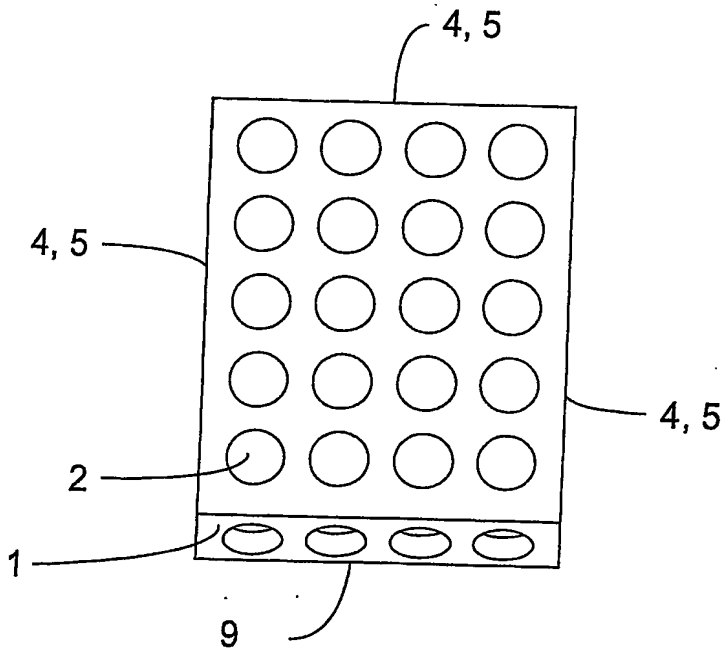


Fig. 1

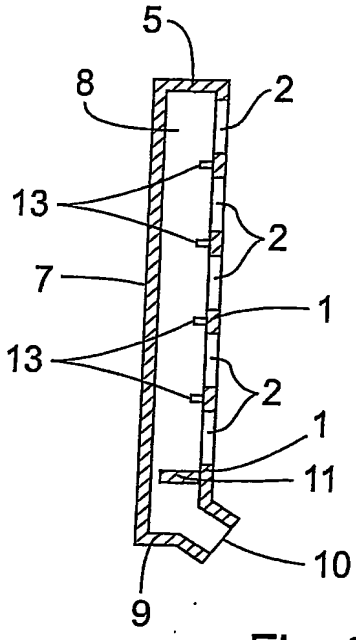


Fig. 2

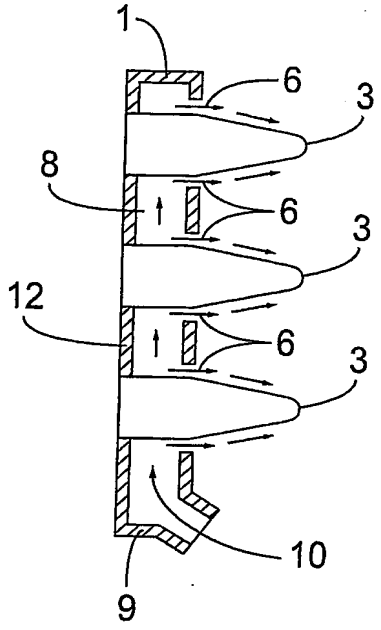


Fig. 3

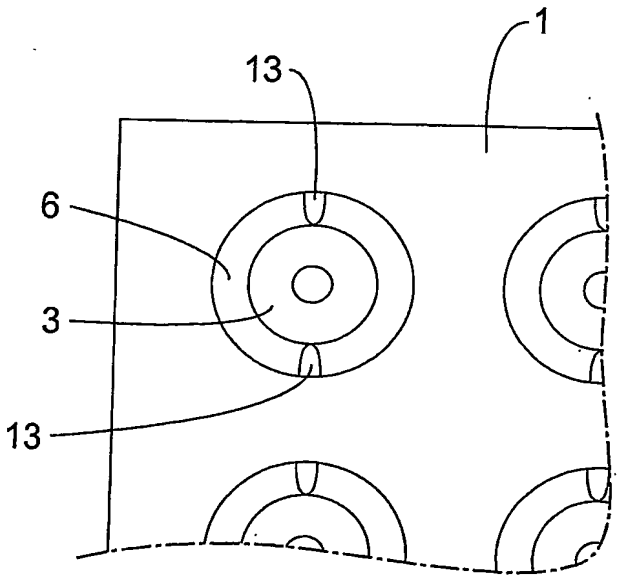


Fig. 4

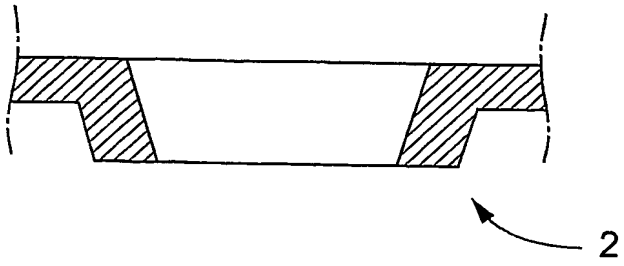


Fig. 5

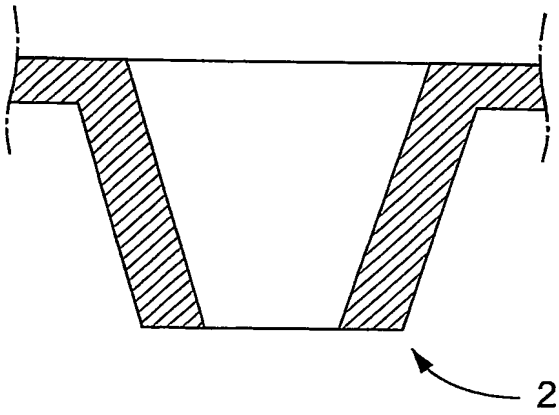


Fig. 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2003/001953

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: B01L 7/00, B01L 3/00
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, WPI DATA, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 1266691 A1 (AIC), 18 December 2002 (18.12.2002), abstract ---	1-6
A	US 5504007 A (JOHN L. HAYNES), 2 April 1996 (02.04.1996), abstract ---	1-6
A	US 5942432 A (DOUGLAS H. SMITH ET AL), 24 August 1999 (24.08.1999), abstract ---	1-6
A	WO 137997 A1 (GLAXO GROUP LIMITED), 31 May 2001 (31.05.2001), abstract ---	1-6

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
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"E" earlier application or patent but published on or after the international filing date
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"P" document published prior to the international filing date but later than the priority date claimed
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"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
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Date of the actual completion of the international search	Date of mailing of the international search report
5 March 2004	10 -03- 2004
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Mats Raidla/mj Telephone No. +46 8 782 25 00

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5716584 A (WILLIAM R. BAKER ET AL), 10 February 1998 (10.02.1998), abstract -- --------	1-6

INTERNATIONAL SEARCH REPORT
Information on patent family members

24/12/2003

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